IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NIPPON SHINYAKU CO., LTD., Plaintiff, v. SAREPTA THERAPEUTICS, INC., Defendant.	C.A. No. 21-1015 (GBW) **DEMAND FOR JURY TRIAL**
SAREPTA THERAPEUTICS, INC. and THE UNIVERSITY OF WESTERN AUSTRALIA, Defendant/Counter-Plaintiffs, v. NIPPON SHINYAKU CO., LTD. and NS PHARMA, INC., Plaintiff/Counter Defendants.	[redacted] [redacted]

PLAINTIFF'S CONCISE STATEMENT OF FACTS IN SUPPORT OF ITS MOTION FOR PARTIAL SUMMARY JUDGMENT NO. 5 REGARDING NO INEQUITABLE CONDUCT

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1. Sarepta and UWA have alleged two bases for their inequitable conduct allegations against each of the patents asserted by NS, the first arising during prosecution of Nippon Shinyaku's U.S. Patent No. 9,708,361 ("the '361 patent") after an alleged failure to disclose data contrary to NS's arguments of unexpected superiority of the claimed antisense oligonucleotides ("AOs") and failure to disclose a paper by Sazani et al. ("Sazani 2010"). Sarepta's Countercls. (D.I. 328), ¶¶ 214-218, 227-230; Ex. 1, ¶¶ 634-635; Ex. 3, ¶¶ 144, 146.

2. Sarepta and UWA did not submit an opening report from their Patent and Trademark Office ("PTO") expert Andrew Hirshfeld on the issue of inequitable conduct. Ex. 14 (Hirshfeld Dep.) at 24:17–20, 26:20–27:1. Sarepta and UWA adduced no direct evidence concerning the specific intent to deceive. The evidence Sarepta and UWA rely upon with respect to deceptive intent comprises of the knowledge of relevant data or references that were not disclosed to the PTO. Ex. 1, ¶¶ 666, 703, 738-744.

PROSECUTION OF THE '361 PATENT

3. The '361 patent was filed as application no. 14/615,504 on February 6, 2015, claiming priority to International Patent Application No. PCT/JP2011/070318, filed August 31, 2011. Sarepta's Countercls. (D.I. 328), ¶ 99.

4. The examiner initially rejected the pending claims, which were directed to a number of AOS complementary to the +31+61 region of exon 53 that cause skipping, and morpholino oligomers with a particular 5' end modification, as unpatentable over "Popplewell et al [US20100168212], Sazani et al [US2010013591] in view of Baker et al [US20130109091] and Bennett et al [US20120190728]." *Id.* at 602-603 (pending claims 1, 19-21), 739. According to the examiner, "[t]he invention includes modifications to the [antisense] compounds where these modifications are well known and routinely utilized in the antisense art at the time of invention." *Id.* at 740. Regarding PMOs, the examiner noted an express disclosure in the Popplewell '212

reference that "the advantage of a PMO is that it has excellent safety profiles. . . ." amongst other desirable characteristics. *Id.* at 741. The examiner noted that the 5' end modifications "recited in the claims were well known and routinely used in the art at the time of invention as shown by the above art and evidence by Baker et al and Bennett et al." *Id.* at 744.

5. In response, the applicants amended the claims to recite two specific sequences: SEQ ID NO. 11 and SEQ ID NO. 57, which were. SEQ ID NO. 11 and 57 were complementary to nucleotides +32 to +56 and +36 to +60 of exon 53, respectively, and argued that the cited references did not teach or suggest these two sequences. *Id.* at 756, 760. Additionally, applicants argued that these two AOs "offer superior skipping effects" over the oligomers taught in the Popplewell and Sazani references based on an indirect comparison between the data shown in various figures of the patent. *Id.* at 761.

6. The examiner issued a Final Rejection maintaining the obviousness rejection. *Id.* at 775. The examiner stated applicant's arguments were "not persuasive" and expressly disagreed with the claim of unexpected superior results on the basis that "[t]he compounds function as designed, to alter splicing." *Id.* at 780, 782. The examiner also noted that two recited SEQ ID NOS. "fall squarely within . . . a 'superior' target region of exon 53" taught by Popplewell, namely +30+59. *Id.* at 778-779.

7. The applicants then made a narrowing amendment to the claims to recite only SEQ ID NO. 57, which targets +36+60 of exon 53, arguing that the sole AO claimed did not fall squarely within Popplewell's top-performing AO targeting +30+59. *Id.* at 788, 791-792. Applicant also reiterated the unexpected results argument for SEQ ID NO. 57 based on Figures 16-17 and 18-19 of the specification. *Id.* at 793.

8. The examiner allowed the claims without providing a statement of reasons for

allowance. Ex. 28 at 803-807. "The most reasonable explanation . . . is that the examiner was persuaded by each of the arguments or all of the arguments that were made." Ex. 14 at 155:2–19.

9. [redacted] Ex. 1, ¶ 655.

10. Dr. Dowdy concedes that he "could not confirm whether NS omitted data from Figures 1-8." Ex. 3, ¶ 149. [redacted] Ex. 13 at 143:1–17; 148:13–18.

11. Dr. Dowdy asserts that the Sazani 2010 reference is material to patentability because it: (i) "disclosed the entire chemical structure of AVI-4658, including the PMO chemical backbone and 5'-TEG modification"; and (ii) "provided detailed safety and genotoxicity information that was not otherwise available." Ex. 1, ¶¶ 736-737.

12. The chemical structure of AVI-4658 is outside the scope of the NS Patent claims. The 5'-TEG modification is disclosed in Sazani '586, a reference that was disclosed to the PTO, and a POSA would be able to utilize Sazani '586 to design AOs. Ex. 13 at 173:10–16. Dr. Dowdy further testified that "[r]eading Popplewell US '212 [a reference expressly relied upon by the examiner] in light of the general knowledge in the art, a POSA as of August 31, 2011 would at once envisage the TEG modification." Ex. 1, ¶ 335. [redacted] Ex. 13. at 173:10–23.

13. Sazani '586 is the same as the Sazani US 2010/0130591 cited by the examiner in rejecting the claims of the '351 patent. Ex. 6 at p. 127, n.23.